DURECT Announces Amendment to Accelerate Ongoing Phase 2a Trial of DUR-928 in Alcoholic Hepatitis (AH) by Allowing Dosing of Severe AH Patients in Parallel to Moderate AH Patients

CUPERTINO, Calif., Nov. 19, 2018 /PRNewswire/ — DURECT Corporation (Nasdaq: DRRX) today announced it has amended its ongoing Phase 2a clinical trial of intravenously administered DUR-928 in patients with alcoholic hepatitis (AH) to accelerate the initiation of dosing of severe AH patents. The Company recently completed dosing for the low-dose 30 mg cohort (n=4) of Part A (moderate AH patients), and with this amendment in place, can now begin enrolling Part B (severe AH patients), starting with the low dose, while it simultaneously continues enrolling Part A at the next higher dose (90 mg). DUR-928, the lead investigational product in the Company's Epigenetic Regulator Program, is an endogenous, first-in-class small molecule, which may have broad applicability in diseases such as nonalcoholic steatohepatitis (NASH) and other disorders of the liver such as Primary Sclerosing Cholangitis (PSC), in acute organ injuries such as acute liver and kidney injury, and in inflammatory skin disorders such as psoriasis and atopic dermatitis.

"This amendment will enable dosing in severe AH patients in parallel to the moderate patients, and we expect it to accelerate the overall timeline for the trial," said James E. Brown, President and CEO of DURECT. "Over the course of the trial, the clinical sites have encountered many severe AH patients who may have qualified for Part B but were deemed screen failures due to their MELD scores being too high to participate in Part A."

The Phase 2a trial is an open label, dose escalation, multi-center U.S. study, originally designed to be conducted in two sequential parts. Part A includes patients with moderate AH (as determined by the Model of End-Stage Liver Disease (MELD) scores, a common scoring system to assess the severity and prognosis of AH patients), and Part B includes patients with severe AH. Three dose levels of DUR-928 (30, 90 and 150 mg) are planned for testing in Part A. Dose escalation is permitted following review of safety and pharmacokinetic (PK) results of the prior dose level by a Dose Escalation Committee (DEC). The target number of patients for the study is 4-6 per dose group. The objectives of this study include safety, PK and pharmacodynamic (PD) signals, as well as measuring the effect of DUR-928 on liver biochemistry and biomarkers. Additional information on the trial design, including eligibility criteria and site locations, can be found at www.clinicaltrials.gov using the NCT Identifier NCT03432260.

About Alcoholic Hepatitis

AH is a syndrome of progressive inflammatory liver injury associated with long-term heavy intake of alcohol, and encompasses a spectrum that ranges from mild injury to severe, life threatening liver damage. The prevalence of AH is estimated to occur in 10-35% of heavy drinkers. According to an article in the Journal of Clinical Gastroenterology (2015 July; 49(6): 506-511), there were over 320,000 hospitalizations related to alcoholic hepatitis in 2010, resulting in hospitalization costs of nearly $50,000 per patient.

About DURECT Corporation

DURECT is a biopharmaceutical company actively developing therapeutics based on its Epigenetic Regulator Program and proprietary drug delivery platforms. DUR?928, a new chemical entity in Phase 2 development, is the lead candidate in DURECT's Epigenetic Regulator Program. An endogenous, orally bioavailable small molecule, DUR-928 has been shown in preclinical studies to play an important regulatory role in lipid homeostasis, inflammation, and cell survival. Human applications may include acute organ injury such as Alcoholic Hepatitis (AH), hepatic and renal diseases such as nonalcoholic steatohepatitis (NASH) and Primary Sclerosing Cholangitis (PSC), and inflammatory skin conditions such as psoriasis and atopic dermatitis. DURECT's advanced oral and injectable delivery technologies are designed to enable new indications and enhanced attributes for small-molecule and biologic drugs. Late stage product candidates in this category include POSIMIR® (bupivacaine extended release solution), an investigational locally-acting, non-opioid analgesic intended to provide up to 3 days of continuous pain relief after surgery, and ORADUR®-Methylphenidate ER Capsules, approved in Taiwan as Methydur Sustained Release Capsules, where it is indicated for

the treatment of attention deficit hyperactivity disorder (ADHD). In addition, for the assignment of certain patent rights related to its drug delivery technology, DURECT will receive single digit sales-based earn-out payments from U.S. net sales of PERSERIS™ (risperidone), which was approved by FDA in July 2018 for the treatment of schizophrenia in adults and is owned and marketed by Indivior PLC. For more information, please visit www.www.durect.com.

NOTE: ORADUR®, POSIMIR® and SABER® are trademarks of DURECT Corporation. Other referenced trademarks belong to their respective owners. DUR-928 and POSIMIR are drug candidates under development and have not been approved for commercialization by the U.S. Food and Drug Administration or other health authorities.

DURECT Forward-Looking Statement

The statements in this press release regarding clinical development plans for DUR-928, including potential acceleration of the Phase 2a trial in AH, potential future payments from Indivior, and the potential benefits and uses of our drug candidates, including the potential use of DUR-928 to treat PSC, AH, other disorders of the liver, kidney diseases, acute organ injuries, psoriasis, atopic dermatitis or other inflammatory conditions are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, the risks that clinical trials of DUR-928 are not started when anticipated, take longer to conduct than anticipated, or do not demonstrate the safety or efficacy of DUR-928 in a statistically significant manner, the risk that Indivior will not launch PERSERIS or that it will obtain marketplace acceptance, the risk that prior clinical trials will not be confirmed in subsequent trials, the potential failure of clinical trials to meet their intended endpoints, the risk that additional time and resources that may be required for development, testing and regulatory approval of DUR-928, potential adverse effects arising from the testing or use of our drug candidates, and risks related to our ability to obtain capital to fund operations and expenses. Further information regarding these and other risks is included in DURECT's Form 10-Q filed on November 8, 2018 under the heading "Risk Factors."

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Michael Arenberg, Chief Financial Officer, DURECT Corporation, 408-346-1052